Spontaneous Thrombosis of an Orbital Arteriovenous Malformation Revealing Hereditary Haemorrhagic Telangiectasia (Rendu-Osler-Weber Disease)

A Case Report

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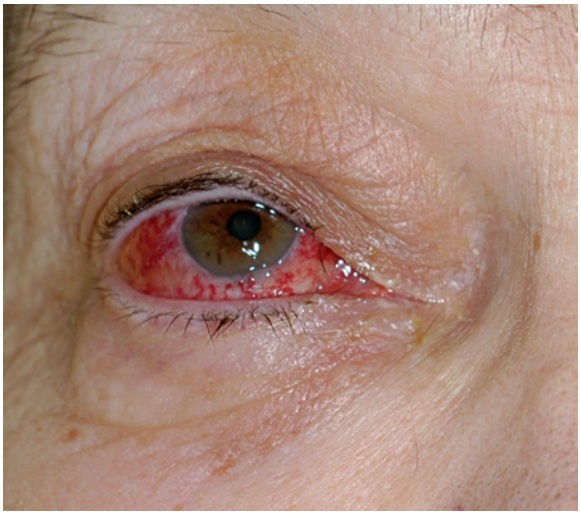
Summary

Hereditary Haemorrhagic Telangiectasia (HHT) is a genetic disorder responsible for cutaneous or mucosal telangiectasia and arteriovenous malformations (AVMs). The most frequent locations are lung and brain. In contrast, orbital AVMs are very rare. We describe a case of symptomatic orbital arteriovenous malformation due to spontaneous thrombosis. A 65-year-old woman was referred for chronic right eye proptosis associated with dilation of conjunctival vessels with a jellyfish pattern. Right visual acuity was 20/40 and intraocular pressure was 40 mmHg. Personal and familial history of recurrent epistaxis, associated with multiple telangiectasia within lips and palate, led to the diagnosis of HHT. Magnetic resonance imaging (MRI) completed with cerebral angiography found a giant and occluded AVM within the right orbit. Other AVMs were also found in brain and chest, confirming the diagnosis. Antiglaucomatous eyedrops were added to reduce intraocular pressure and a steroid therapy was begun. Two months later, visual acuity decreased in the right eye, due to a central retinal vein thrombosis. In conclusion, Most brain or pulmonary AVM can be treated by embolization. By contrast, this treatment in case of orbital location can lead to central retinal artery and/or central retinal vein occlusion, which may also appear as a spontaneous complication of the orbital AVM. Therapeutic management of orbital AVM is thus not standardized, and the balance between spontaneous and iatrogenic risk of visual loss has to be taken into account.

Introduction

Hereditary haemorrhagic telangiectasia (HHT) was first recognized in the 19th century as a familial disorder causing nosebleeds, gastrointestinal bleeding, and abnormal vascular structures. The combination of these clinical findings with iron deficiency anaemia, characteristic telangiectasia on the lips, oral mucosa, and fingertips has become firmly established as a medical entity named Rendu-Osler-Weber disease or HHT. Yet this clinical scenario constitutes only one of the presentation patterns of HHT, and may not be obvious in HHT patients who still have life-threatening manifestations of disease. It is now recognized that in addition to the above-mentioned microscopic mucocutaneous telangiectasias derived from post capillary venules, HHT can also lead to the development of abnormal vascular structures at other



↑ *Figure 1* Conjunctival chemosis, with dilated conjunctival vessels, giving a jellyfish pattern.

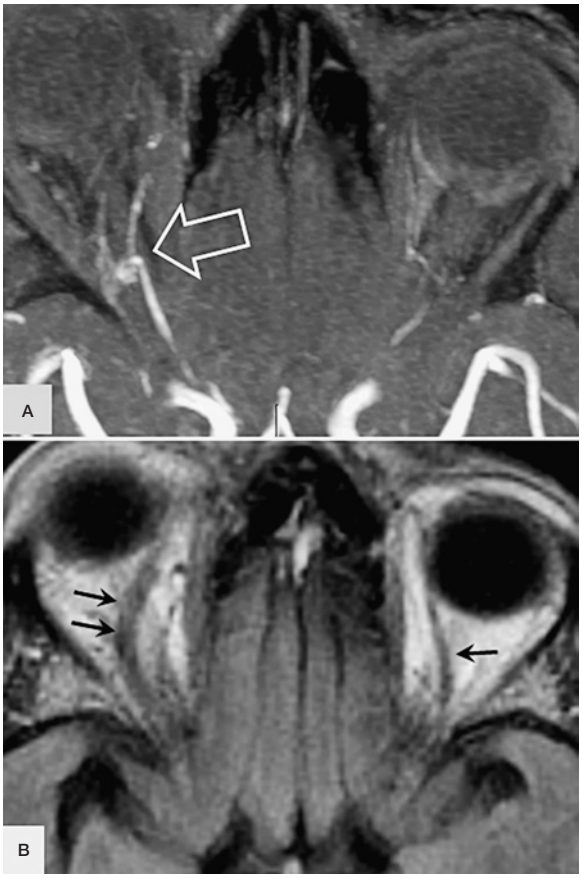


Figure 2 Axial MRI in Time of Flight (TOF) (A) → and FLAIR (B) sequences of the orbit showing right proptosis. TOF sequence shows an abnormal vascular arterial network in the orbit fed by the right ophthalmic artery (A: empty arrow) compared to the other side, due to the MAV. The right ophthalmic vein is dilated (B: double arrows) match to normal size in the left side (B: single arrow).

sites. Arteriovenous malformations (AVMs) in the pulmonary, cerebral, and hepatic circulations account for some of the most devastating clinical complications of the disease. Therefore, this disease can and should no longer be regarded as a rare and benign disease, and physicians dealing with patients suspected of having HHT should be aware of the possibly life-threatening clinical manifestations of HHT.

The far most frequent ophthalmic manifestations of HHT are conjunctival telangiectasia, which are rarely symptomatic. We describe a case of a symptomatic orbital arteriovenous shunt. Based on this case report, we present a review of the spectrum of vascular lesions due to HHT expressed in the orbital and ocular fields.

Case Report

A 65-year-old woman was referred to our department for proptosis of the right eye, lasting for six months and associated with a progressive decreased visual acuity for two months. The patient described recurrent epistaxis occurring several years ago, five late spontaneous miscarriages and multiple episodes of gastric bleeding. Additionally, her mother also suffered from recurrent epistaxis. Despite this medical and familial history, no work-up had been previously done. At arrival, best corrected visual acuity of her right eye was 20/40. Slit lamp examination disclosed a conjunctival chemosis with dilated conjunctival vessels, leading to a jellyfish pattern (Figure 1). The right intraocular pressure was 40 mmHg. Fundus of the right eye was normal, as was examination of the left eye. Multiple mucocutaneous telangiectasia were found, especially on the lips and palate, with a shape very suggestive of HHT. Magnetic resonance imaging (MRI) confirmed the exopthalmia (grade 2) with ocular muscles enlargement. Time of flight and gadolinium sequences showed vascular flow refer to a possible arteriovenous shunt located in the orbit (Figure 2). Angiography was subsequently performed and showed an arteriovenous malformation mainly fed by the ophthalmic artery and draining into intra-orbital venous drainage with occlusion of the ophthalmic vein (Figure 3). Two micro

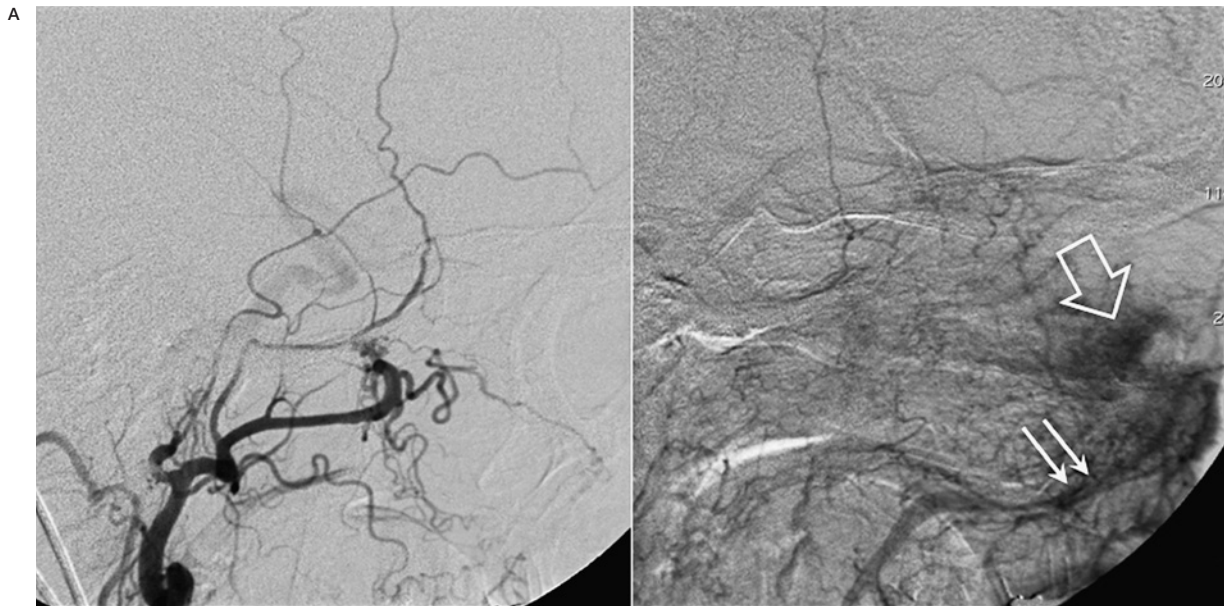


Figure 3 Left maxillary artery angiogram. Arterial phase (A) shows no component from the middle meningeal artery or the distal maxillary artery. On the venous phase (B) the superior and the inferior ophthalmic veins are not opacified. The facial vein (double arrows) is draining the nasal fossa, supporting the hypothesis of superior ophthalmic vein thrombosis. Note the telangiectasia of the nasal cavity (empty arrow).

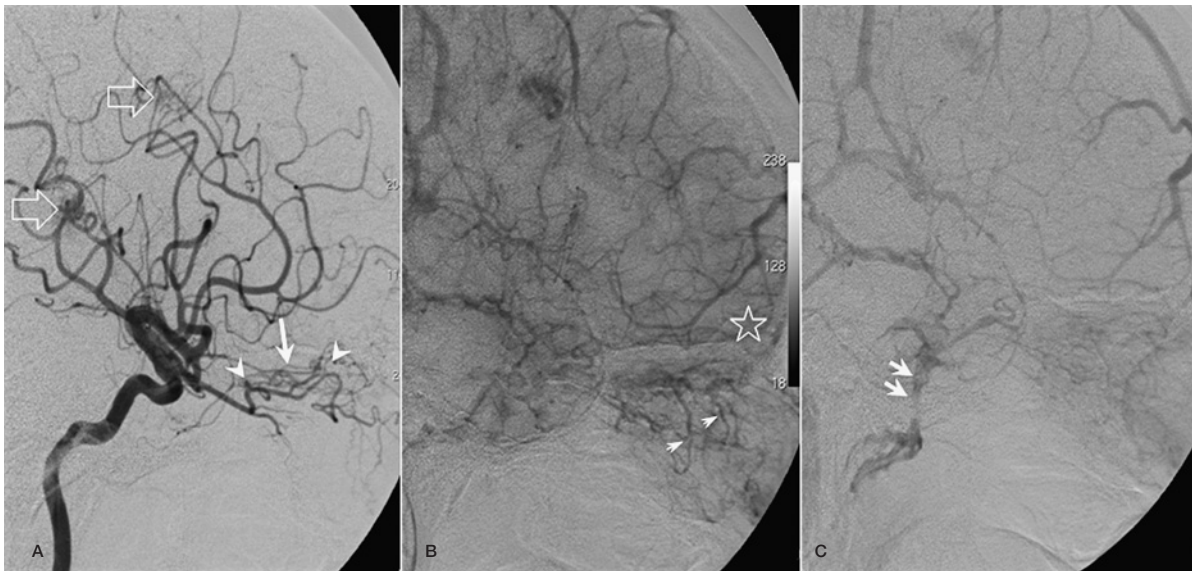


Figure 4 Internal carotid angiography in lateral view (A: arterial phase; B; early venous phase, C: late venous phase). Posterior and anterior ethmoidal network (A: arrowheads) are partially opacifying the superior ophthalmic vein (A: arrow), with hyperaemia and venous stagnation (B: star). This supported the diagnosis of arteriovenous shunt with thrombosis of the draining vein. Anastomotic veins (B: small arrows) look congestive. The cavernous sinus is patent and drains the superficial middle cerebral vein (C: double arrows). Note the two cortical cerebral microarteriovenous malformations (A: empty arrows).

AVMs (smaller than 1 cm) were found in the cortical territories of both right sylvian and right anterior cerebral arteries (Figure 4). In the lung, six pulmonary AVMs were found with an indication for preventive embolization. Liver vessels were normal.

The treatment included steroid therapy, initially with high doses of intravenous methylprednisolone (500 mg per day for three days) before oral prednisolone (60 mg per day for 20 days tapered off) to decrease the inflammatory part of the lesion. Antiglaucomatous eyedrops (dorzolamide, timolol and latanoprost) were added to reduce intraocular pressure. Proptosis gradually resolved and intraocular pressure normalized. However, two months after the initial improvement, the visual acuity suddenly decreased in the right eye. Eye fundus examination found signs of central retinal vein thrombosis, with severe retinal ischemic lesions leading to irreversible damage of the photoreceptor cells. Final right best corrected visual acuity was limited to counting fingers.

Discussion

Hereditary Haemorrhagic Telangiectasia (Rendu-Osler-Weber's disease) is a familial disease leading to systemic abnormalities of post capillary venules. The transmission of HHT is autosomal dominant, with variable penetrance. Two mains mutations on chromosome 9 (HTT1) and 12 (HTT2) have been identified in the genes encoding the endoglin and the activin receptor-like kinase, respectively [1]. Vascular involvement can be mucocutaneous telangiectasia, small arteriovenous malformation or large high-flow arteriovenous fistula. The clinical diagnosis is based on the association of multiple criteria (first degree of hereditary, spontaneous recurrent nosebleeds, mucocutaneous telangiectasias typically located within lips, oral cavity, fingers or nose, visceral involvement such as pulmonary, central nervous system or hepatic AVMs).

The clinical settings of HHT are heterogeneous, and may affect many organs. Telangiectasia of the nasal mucosa leading to spontaneous and recurrent epistaxis is the most common clinical manifestation [2]. Visceral involvement is less common but consequences can be more serious in case of bleeding. Gastrointestinal haemorrhage is the second most frequent form of bleeding [3]. Liver involvement is reported in up to 30% of persons with HHT [4-5], while pulmonary arteriovenous malformations affect 24% of patients [6], possibly leading to hypoxaemia due to high-flow arteriovenous fistula. Arteriovenous malformation may also involve the spinal cord or the brain in 10% of patients [7]. Micro-AVMs typically occur in adults and are not reported as subject to bleeding. Larger AVMs, named nidus and located in the cortex, may lead to haemorrhage. High flow macrofistulae are typically revealed during childhood, due to seizures or cardiac insufficiency [8]. The prognosis of HHT is ruled by the location and the size of AVMs. Endovascular management is a common treatment for AVM, especially for brain locations [9].

Ocular involvement of HHT can affect several ocular tissues. Conjunctival telangiectasia is the most frequent manifestation, accounting for 35 to 38 % of ocular locations [10-11]. By contrast, retinal involvement is very rare, with only four cases previously reported [10,12-13]. Lesions differed among patients (temporal telangiectasia with haemorrhage, retinal arteriovenous shunt, network of telangiectasia vessels adjacent to the optic disk without haemorrhage, tortuosity of the retinal vasculature). In those cases, visual loss did not occur. Only one case of choroidal location has been reported in the literature, leading to choroidal haemorrhage during vitreoretinal surgery for retinal detachment [14].

We describe here a case of HHT-related orbital AVM leading to ocular manifestations (proptosis, chemosis and ocular hypertension). Orbital AVMs have been reported in patients without HHT [15-17]. This type of AVM is rare and may cause similar symptoms to those associated with a cavernous sinus dural AVM [16]. Subacute or chronic orbital arteriovenous fistulae associated with increased intraocular pressure have already been described [18-19]. Orbital dural arteriovenous shunts out of the cavernous sinus, with venous drainage into the orbit have been described and typically have a slow flow. Supraselective angiography is often required to confirm the diagnosis and to establish the curative strategy. In most cases, endovascular embolization is not possible due to the very small size of the arterial feeder and the risk for vision, since there may be some anastomoses with the central retinal artery [20]. The close match between orbital AVM and ophthalmic vessels explains potential complications on visual function when embolization is performed.

In our patient, thrombosis of the arteriovenous malformation led to a decrease of the

venous outlets flow associated with congestion and inflammation responsible for the ocular symptoms (proptosis, chemosis and ocular hypertension). Usually, treatment of thrombosis is based on anticoagulation, while embolization is used to reduce the size of AVMs inducing thrombosis. In our case, spontaneous thrombosis was a kind of treatment of the lesion. Conservative treatment (i.e. steroid therapy) succeeded in reducing orbital symptoms. A conservative approach was chosen since the arteriovenous shunt was no longer patent. From a theoretical point of view the embolization could have been performed conserving the central artery of the retina, since the feeding artery was arising after the second portion (bend over the optic nerve) of the opththalmic artery.

Concerning the spontaneous occlusion of orbital arteriovenous malformations, we lack reports in the literature evaluating the natural history and spontaneous occlusion. If we consider the pial brain location of arteriovenous malformations, the incidence of spontaneous obliteration (rather than spontaneous thrombosis) is reported between 0.8% and 20% [21]. We did not assess any cerebrofacial arteriovenous metameric syndrome (CAMS) in this case of multiple orbital and cerebral arteriovenous malformations, since the cerebral arteriovenous malformations were not diencephalic (CAMS 2 is associated optic nerve AVM with diencephalic AVM) [22] and since multiple cerebral arteriovenous malformations in HHT are very frequent (45%) [23].

Conclusion

Hereditary Haemorrhagic Telangiectasia (HHT) (Rendu-Osler-Weber's disease) rarely affects the orbit responsible for ocular symptoms with potential proptosis, chemosis and ocular hypertension. In the present case, HHT disease was revealed by an AVM thrombosis leading to venous congestion. Evolution at two months was complicated by retinal venous occlusion linked to a defect in retinal venous drainage.

In HHT, most brain or pulmonary AVMs can be cured by embolization. By contrast, this treatment in case of orbital location can lead to central retinal artery and/or central retinal vein occlusion, which may also appear as spontaneous complications of the orbital AVM.

Hence the management of orbital AVM cannot be standardized, and the balance between spontaneous and iatrogenic risk of visual loss has to be taken into account for optimal treatment. Ophthalmologist and neuroradiologist have to be aware of possible orbital AVM in HHT.

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